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Left ventricular performance in children with homozygous sickle cell anaemia[1]

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SUMMARY Left ventricular performance was determined by echocardiography in 44 black children with homozygous sickle cell anaemia and a control group of 28 normal black children of comparable age. Statistically significant differences were observed between the children with sickle cell anaemia and the normal group in left ventricular ejection fraction (sickle cell anaemia group: 0·59 ± 0·01 [mean ± standard error of the mean] vs. normal group: 0·65 ± 0·01), cardiac index (5·3 ± 0·3 vs 4·2 ± 0·3 l/min per m^2), mean circumferential fibre shortening velocity (1·16 ± 0·04 vs 1·31 ± 0·03s^{-1}) and the percentage of shortening of left ventricular minor axis dimension (32·5 ± 1 vs 36·7 ± 0·8). The children with sickle cell anaemia were divided into two groups according to the absence or presence of dyspnoea and/or fatigue on moderate effort; though both groups had the same degree of anaemia, significantly depressed left ventricular performance indices were observed only in the group of symptomatic patients. All asymptomatic children with sickle-cell anaemia had uncompromised left ventricular performance.

These findings indicate that left ventricular dysfunction is present in a significant proportion of children with sickle cell anaemia. The extent of the left ventricular dysfunction, is not related to the degree of anaemia or the percentage of fetal haemoglobin. Since many of the symptoms, physical signs, and radiological findings of severe anaemia resemble those of congestive heart failure, echocardiographic examination of symptomatic children with homozygous sickle cell anaemia is useful in detecting the presence of left ventricular dysfunction.

Children and adults with homozygous sickle cell anaemia frequently present evidence of cardiovascular system abnormalities (Klinefelter, 1942; Winsor and Burch, 1945; Wintrobe, 1946; Shubin *et al.*, 1960; Uzsoy, 1964; Ng *et al.*, 1967). The reduced haemoglobin content in conjunction with the pulmonary dysfunction (Moser and Shea, 1957; Moser *et al.*, 1960; Femi-Pearse *et al.*, 1970) observed in these subjects causes chronic arterial hypoxaemia (Jensen *et al.*, 1957; Sproule *et al.*, 1957) and a compensatory high cardiac output state (Brannon *et al.*, 1945; Leight *et al.*, 1954; Sproule *et al.*, 1958; Varat *et al.*, 1972). It is postulated that the excessive work load chronically imposed on the heart by the high cardiac output, in conjunction with the tendency of the sickle cells to occlude small vessels in the systemic, pulmonary (Moser *et al.*, 1960), and coronary circulation (Oliveira and Gomez-Patino, 1963; Rubler and Fleischer, 1967) may result in left ventricular dysfunction in the absence of other cardiac abnormalities. However probable, this hypothesis has not yet been adequately documented (Lindsay *et al.*, 1974). Recent noninvasive studies have failed to identify left ventricular dysfunction in adults with sickle cell anaemia (Gerry *et al.*, 1976). This study was designed to evaluate the performance of the left ventricle in children with sickle cell anaemia.

Subjects and methods

Forty-four black children, whose ages ranged from 2 to 14 (mean 8·6 ±0·4) years, with homozygous sickle cell anaemia documented by haemoglobin electrophoresis (SS haemoglobin), and a control group of 28 randomly selected normal black

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children of comparable age (range 3 to 16, mean 7·8 ±0·7 years, P >0·05) had echocardiographic evaluation of left ventricular function. History, physical examination, electrocardiogram, and chest *x*-ray were obtained on all patients. The following haematological data were also obtained: haemo-

Table 1 *Clinical and noninvasive data of 44 patients with homozygous sickle cell anaemia*

Case	*Age/sex (y)*		*C/T (>0·5)*	*Hct*	*Hb*	*%FHb*	*HR*	*ET*	*BSA*	*Dd/m²*	*Ds/m²*	*CI*	*%ΔD*	*EF*	*Vcf*
Group 1															
1	10	M	—	17	6·3	3·4	86	300	1·00	47	28	6·7	40	0·68	1·35
2	9	M	—	27	9·5	0·6	80	290	0·98	40·8	26·5	4·0	35	0·62	1·21
3	13	F	+	19	6·7	7·0	83	320	1·64	31·7	20·1	4·6	37	0·64	1·14
4	11	M	+	29	9·4	12·0	70	310	1·06	42·4	28·3	4·1	33	0·60	1·07
5	4	F	—	26	8·9	21·0	80	300	0·70	61·4	38·5	6·8	37	0·65	1·24
6	5	M	—	27	9·4	21·0	103	280	0·66	62·1	42·4	7·5	32	0·58	1·13
7	14	F	+	23	7·2	4·6	66	340	1·37	36 4	21 8	4 3	40	0·68	1·18
8	10	M	—	30	9·6	16·9	71	275	0·96	46·8	30·2	4·7	35	0·63	1·29
9	5	M	—	—	6·8	5·1	60	250	0·76	50·0	34·2	3·2	32	0·58	1·26
Mean	9			24·7	8·2	10·2	78	296	1·01	46·5	30·0	5·1	35·7	0·63	1·21
±SEM	1·2			1·7	0·5	2·6	4	9	0·11	3·4	2·4	0·5	1	0·01	0·03
Group 2															
10	10	M	+	18	6·5	3·0	107	260	0·82	47·5	29·2	6·4	39	0·66	1·48
11	7	M	+	24	7·8	6·0	106	260	0·84	59·5	40·4	9·7	32	0·59	1·23
12	10	M	+	21	6·9	4·0	80	300	0·94	44·6	29·7	4·5	33	0·60	1·11
13	7	F	+	18	6·5	4·0	101	250	0·88	47·7	27·2	7·1	43	0·71	1·72
14	7	M	+	29	7·4	5·0	103	260	0·88	44·3	26·1	6·0	41	0·69	1·58
15	9	F	+	26	7·5	1·0	80	300	1·08	48·1	27·7	7·5	42	0·70	1·41
16	12	M	+	21	7·2	3·4	90	270	1·09	44·9	25·6	7·3	43	0·71	1·59
17	2	M	+	20	7·2	9·0	127	230	0·54	55·5	35·1	6·2	37	0·64	1·60
18	8	M	+	24	7·8	4·7	82	280	0·86	55·8	38·3	6·6	31	0·58	1·12
19	7	M	+	25	8·3	7·5	91	280	0·96	47·9	33·3	5·8	30	0·57	1·09
20	9	M	+	24	8·0	7·0	82	290	0·88	44·3	26·1	4·8	41	0·69	1·42
21	4	M	+	23	7 4	—	115	260	0 69	55·0	36·2	7·1	34	0·61	1·31
22	7	F	+	24	7·6	7·0	95	300	0·71	56·3	35·2	6·8	37	0·65	1·25
23	9	F	+	25	8·4	13·4	100	300	1·16	41·3	28·4	5·9	31	0·57	1·04
24	14	F	+	23	7·3	3·0	83	320	1·10	32·1	20·5	2·8	36	0·63	1·13
25	12	M	—	30	9·6	3·0	88	230	1·12	35·7	25·0	3·5	30	0·56	1·30
26	7	M	+	21	7·2	—	86	280	0·70	62·8	35·7	8·5	43	0·71	1·54
27	5	F	+	29	7·4	—	133	250	0·72	56·9	38·8	8·9	32	0·58	1·27
28	6	F	+	28	8·8	2·0	100	270	0·84	48·8	30·9	6·3	37	0·64	1·36
29	8	M	+	25	8·6	3·0	68	290	1·12	41·0	26·7	4·0	35	0·62	1·20
30	10	M	+	19	6·3	1·6	90	300	0·70	57·9	40·2	5·9	31	0·57	1·02
31	10	M	+	25	8·3	8·0	88	290	0·96	45·8	32·2	5·0	30	0·56	1·02
32	9	F	+	26	8·5	3·0	73	300	0·98	41·8	29·5	3·4	29	0·55	0·98
33	5	M	+	21	7·2	9·0	110	255	0·78	52·5	41·0	5·3	22	0·45	0·86
34	8	M	+	24	7·8	5·0	80	290	0·87	49·4	39·0	3·7	21	0·44	0·73
35	10	F	+	24	7·9	10·0	60	300	1·00	45·0	32·0	3·4	29	0·54	0·96
36	5	F	+	19	6·7	2·6	96	290	0·71	59·1	43 6	6·1	26	0·51	0·90
37	10	M	+	24	8·1	10·0	115	235	1·06	46·2	35·8	6·2	23	0·46	0·96
38	9	F	+	30	10·0	18·0	79	290	1·06	41·5	30·1	3·8	27	0·53	0·95
39	8	F	+	30	10·1	8·2	75	310	0·92	43·4	32·6	3·1	25	0·49	0·80
40	9	F	+	28	9·4	12·0	74	290	0·90	45·0	32·2	3·6	28	0·54	0·98
41	13	M	+	21	6·9	2·0	70	300	1·21	41·3	33·0	3·2	20	0·43	0·67
42	12	M	+	21	7·1	3·0	100	300	1·26	34·1	26·1	3·5	23	0·47	0·78
43	11	M	+	22	7·5	16·5	63	290	1·34	30·6	24·6	1·6	20	0·42	0·68
44	8	F	+	21	6·9	12·5	95	270	0·88	44·3	32·9	4·0	26	0·50	0·95
Mean	8·5			23·8	7·8	6·5	91	280	0·93	47·1	32·0	5·4	31·6	0·58	1·14
±SEM	0·4			0·6	0·2	0·8	3	4	0·03	1·3	0·9	0·3	1·2	0·01	0·05
P (1 vs 2)	NS			NS	NS	NS	<0·05	NS	NS	NS	NS	NS	NS	NS	NS
Groups 1+2															
Mean	8·6			24	7·9	7·3	88	283	0·95	47	31·6	5·3	32·5	0·59	1·16
±SEM	0·4			*·6	0·2	0·9	3	4	0·03	1·3	0·9	0·3	1	0·01	0·04

C/T, cardiothoracic ratio; Hct, haematocrit (%); Hb, haemoglobin (g/dl); %FHb, per cent fetal haemoglobin; HR, heart rate (beats/min); ET, left ventricular ejection time (ms); BSA, body surface area (m^2); Dd/m^2, left ventricular end-diastolic dimension index (mm/m^2); Ds/m^2 left ventricular end-systolic dimension index (mm/m^2); CI, cardiac index (l/min per m^2); %ΔD, per cent of shortening of minor axis LV dimension during systole; EF, ejection fraction; Vcf, mean rate of circumferential fibre shortening (s^{-1}); SEM, standard error of the mean; M, male; F, female; NS, statistically insignificant difference.

globin, haematocrit and percentage of fetal haemoglobin. On the basis of symptomatology the patients with sickle cell anaemia were divided into two groups. Group 1 consisted of 9 patients who were completely asymptomatic. Group 2 consisted of 35 patients with dyspnoea and/or fatigue at rest or initiated (or aggravated) by ordinary physical activity. Only one patient of group 2 (case 44, Table 1) was receiving maintenance digitalis.

Echocardiographic examination was performed by use of a Smith Kline Ekoline 20 ultrasonoscope interfaced with a Honeywell fiberoptic strip-chart recorder. A 2·25 MHz focused (5 cm) transducer with an active crystal diameter of 1·27 cm was used. The children were studied in the supine position and the transducer was positioned along the left sternal border at that intercostal space (3rd to 5th, usually the 4th), from which a strong mitral valve echo was visualised, with the transducer pointed perpendicularly to the chest wall with slight medial but no superior or inferior angulation (Popp *et al.*, 1975). From this position, the transducer was slowly tilted in an inferior and lateral direction, until the echoes of the mitral valve were replaced by those of the chordae tendineae; at this level the echogram was recorded after minor adjustments in transducer angulation and/or gain control, aimed at providing optimal visualisation of the endocardial echoes from both the posterior left ventricular wall and the left side of the interventricular septum.

The left ventricular end-diastolic dimension (Dd) was measured as the vertical distance between the left septal echo and the left ventricular endocardial echo at the onset of the QRS complex of the electrocardiogram (Meyer *et al.*, 1975). The left ventricular end-systolic dimension (Ds) was measured at the point of maximal approximation of the interventricular septum and the posterior left ventricular wall. Using these echocardiographic dimensions, the percentage shortening in the echocardiographic minor dimension of the left ventricle was calculated as (Fortuin *et al.*, 1972):

$$\%\,\Delta D = (Dd - Ds) \times 100/Dd$$

and the normalised mean rate of circumferential fibre shortening was calculated as (Paraskos *et al.*, 1971; Cooper *et al.*, 1972; Quinones *et al.*, 1974):

$$\text{mean Vcf } (s^{-1}) = (Dd - Ds)/ET \times Dd$$

where ET was the left ventricular ejection time measured from the onset of the rapid upstroke to the nadir of the dicrotic notch of the external carotid pulse tracing.

Echocardiographic estimation of the left ventricular end-diastolic volume was obtained using the following regression equation (Meyer *et al.*, 1975):

$$EDV = -19{\cdot}2 + 14{\cdot}58\ Dd + 0{\cdot}62\ Dd^3$$

The left ventricular ejection fraction (EF) was estimated from the echocardiographic left ventricular dimensions (Dd, Ds) using the mathematical relation previously described by Meyer *et al.* (1975)

$$EF = 1 - \frac{As}{Ad} \cdot \left(\frac{Ds^2}{Dd}\right)$$

where the factor $\frac{As}{Ad} = 0{\cdot}90$, is the ratio of end-systolic/end-diastolic left ventricular major axis dimension corresponding to an assumed 10 per cent shortening of this axis.

The product (EDV × EF), representing the stroke volume, was multiplied by the heart rate to provide the cardiac output which was then indexed for body surface area. All measurements were averaged over five arrhythmia-free cardiac cycles.

Student's t test for non-paired data was used for statistical comparison of the results between groups; all values are given as mean ± standard error of the mean. Correlation coefficient (r) analysis was carried out by the least square method. The level of statistical significance was set at $P < 0{\cdot}05$.

Results

Clinical, radiographic, haematological, and echocardiographic data for the two groups of patients with sickle cell anaemia are listed in detail in Table 1. Statistical analysis of the mean values for the echocardiographic indices of left ventricular performance in the two groups of patients with sickle cell anaemia as well as in the group of normal control subjects is presented in Table 2.

As can be seen in Table 1, there was no significant difference in age, haemoglobin content, or per-

Table 2 *Echocardiographic indices of left ventricular performance in 28 normal children and two groups (1 and 2) of patients with homozygous sickle cell anaemia*

	Dd/m² *(mm/m²)*	*CI* *(l/min per m²)*	%ΔD	*EF*	*Vcf* *(s^{-1})*
Normal (n=28)	40·4 ±1·8	4·2 ±0·3	36·7±0·8	0·65 ±0·01	1·31 ±0·03
Group 1 (n=9)	46·5* ±3·4	5·1* ±0·5	35·7* ±1	0·63* ±0·01	1·21* ±0·03
Group 2 (n=35)	47·1‡ ±1·3	5·4† ±0·3	31·6‡1·2	0·58§ ±0·01	1·14† ±0·05

Abbreviations; Same as in Table 1. All values are expressed as mean ±standard error of the mean.
*Statistically insignificant ($P > 0{\cdot}05$) difference in comparison with normal group or group 2.
†$P < 0{\cdot}01$ in comparison with normal group.
‡$P < 0{\cdot}005$ in comparison with normal group.
§$P < 0{\cdot}001$ in comparison with normal group.

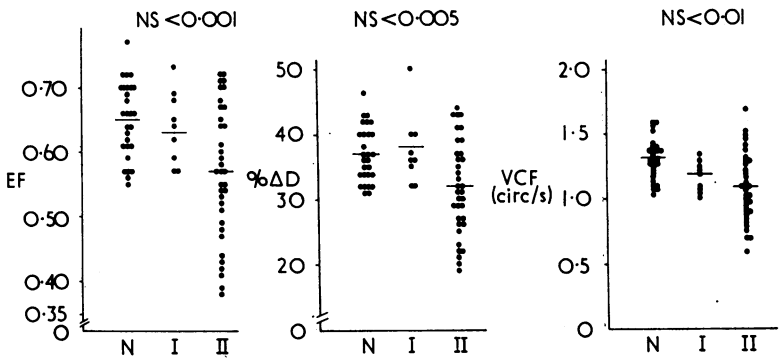

Fig. *Diagrammatic representation of the echocardiographic left ventricular performance indices found in 9 asymptomatic (1) and 35 symptomatic (2) patients with homozygous sickle cell anaemia, and a control group of 28 normal children (N). The small horizontal bars represent mean values for each group. EF, ejection fraction; % ΔD, per cent shortening of left ventricular minor axis dimension; Vcf, mean rate of circumferential fibre shortening; NS, statistically insignificant difference in comparison with normal group; <0·01 and <0·05 signify the P value for the respective group 1 or 2 in comparison with normal group.*

centage of fetal haemoglobin between the two groups of patient with sickle cell anaemia. The cardiothoracic ratio on upright chest film exceeded 0·50 in 34 of the 35 symptomatic patients of group 2 and in only 3 of the 9 asymptomatic patients of group 1.

In comparison with the group of normal subjects, the symptomatic patients of group 2 had significantly higher values for left ventricular end-diastolic dimension and cardiac index but the left ventricular performance indices (% ΔD, EF, and mean Vcf) were significantly depressed in this group 2 (Table 2). Directionally similar deviations in all these variables from normal were also observed in the asymptomatic patients of group 1, but the values in this group were not statistically different when compared with either the normal group or the symptomatic group 2 (Table 2).

The Figure is a graphic representation of left ventricular performance indices seen in the normal group, and the two groups of patients with sickle cell anaemia. In the normal group per cent ΔD ranged from 30 to 46 ($36·7 \pm 0·8$); the ejection fraction ranged from 0·55 to 0·77 ($0·65 \pm 0·01$); and the mean Vcf ranged from 1·04 to 1·60 ($1·31 \pm 0·03\ s^{-1}$). The asymptomatic patients of group 1 could not be distinguished from the normal group because of the almost complete overlap in the values of left ventricular performance indices between the two groups. Similar, but partial overlap was also present among group 2 and the normal group with respect to the performance indices.

Table 3 *Statistical comparison of clinical, laboratory, and noninvasive data between asymptomatic group 1 and two subgroups (2a and 2b) of symptomatic patients with sickle cell anaemia*

	Group 1 (n=9)	*Group 2 2a (n=20)*	*2b (n=15)*	*P< 1 vs 2a*	*1 vs 2b*	*2a vs 2b*
Age (y)	9 ±1·2	8 ±0·6	9·1 ±0·6	NS	NS	NS
Haematocrit (%)	24·7 ±1·7	23·9 ±0·8	23·7 ±0·9	NS	NS	NS
Haemoglobin (g/dl)	8·2 ±0·5	7·7 ±0·2	7·9 ±0·3	NS	NS	NS
% Fetal haemoglobin	10·2% ±2·6	5·1% ±0·7	8·1% ±1·3	NS	NS	0·05
Heart rate (beats/s)	78 ±4	96 ±4	85 ±4	NS	NS	NS
Ejection time (ms)	296 ±9	274 ±6	287 ±5	NS	NS	NS
Body surface area (m^2)	1·01 ±0·11	0·89 ±0·04	0·98 ±0·05	NS	NS	NS
Dd/m^2 (mm/m^2)	46·5 ±3·4	48·5 ±1·8	45·2 ±2	NS	NS	NS
Ds/m^2 (mm/m^2)	30 ±2·4	30·81·2	33·7 ±1·4	NS	NS	NS
Cardiac index (l/min per m^2)	5·1 ±0·5	6·3 ±0·4	4·1 ±0·3	NS	NS	NS
% ΔD	35·7 ±1	36·4 ±1	24·3 ±1	NS	0·001	0·001
Ejection fraction	0·63 ±0·01	0·64 ±0·01	0·50 ±0·01	NS	0·001	0·001
Mean Vcf (s^{-1})	1·21 ±0·03	1·34 ±0·04	0·88 ±0·03	NS	0·001	0·001

NS, statistically insignificant difference in mean values. Other abbreviations as in Table 1.

For purposes of further analysis group 2 was divided into two subgroups according to the absence (2a) or presence (2b) of left ventricular dysfunction. Subgroup 2a comprised 20 patients (cases 10 to 29, Table 1) who had values for all three left ventricular performance indices equal to or higher than the lowest respective values observed in the normal group; and subgroup 2b consisted of the remaining 15 patients of group 2 (cases 30 to 44, Table 1) who had values for one or more of the three performance indices lower than the lowest respective values noted in the normal group. Thus, on the basis of echocardiographic criteria of left ventricular performance, subgroup 2b was completely separated from the normal group, the symptomatic subgroup 2a, and the asymptomatic group 1. Subgroup 2b could not be distinguished (t test) from subgroup 2a or from group 1 of anaemic patients on the baisis of any of the following variables: age, haematocrit, haemoglobin concentration, heart rate, ejection time, body surface area, and the left ventricular end-diastolic and end-systolic dimension indices (Table 3). The difference in percentage of fetal haemoglobin between subgroup 2b (8·1% ± 1·3) and subgroup 2a (5·1% ±0·7) was statistically significant but too small in absolute amount to support the hypothesis that increased concentration of fetal haemoglobin may be responsible for the depression in left ventricular performance seen in subgroup 2b, particularly since the asymptomatic patients of group 1 had an even higher percentage of fetal haemoglobin (10·2% ±2·6) than subgroup 2b without any clinical or echocardiographic evidence of left ventricular failure (Table 3).

Correlation coefficient (r) analysis involving all 44 patients with sickle cell anaemia failed to provide a significant relation between each of the three indices of anaemia (haematocrit, haemoglobin content, and percentage of fetal haemoglobin) and any of the indices of left ventricular performance (% ΔD, ejection fraction, and mean Vcf).

Discussion

Since severe anaemia and congestive heart failure have many clinical symptoms and physical signs in common (Eichna, 1960), clinical recognition of the presence of heart failure in patients with severe sickle cell anaemia is difficult. Evaluation of left ventricular performance in patients with uncomplicated sickle cell anaemia is hampered by the fact that, in the absence of clinical evidence of coexisting congenital or acquired cardiac abnormalities, cardiac catheterisation is rarely indicated in these patients. As a consequence, the presence of depressed function of the chronically volume overloaded left ventricle in sickle cell anaemia is still controversial (Oliveiria and Gomez-Patino, 1963; Rubler and Fleischer, 1967; Lindsay *et al.*, 1974; Gerry *et al.*, 1976). Experience from other chronic anaemias or anatomical defects representing high output state specifically for the left ventricle, e g. aortic regurgitation, has shown that the overloaded left ventricle is capable of tolerating these conditions for a very long time without haemodynamically detectable evidence of dysfunction. As in all these conditions, the left ventricle in sickle cell anaemia is chronically overloaded but, in contrast to them, sickle cell anaemia presents two additional features which may compromise the function, and accelerate the appearance of failure, of the left ventricle. These factors are: (a) the distinct shift of the oxygen dissociation curve to the right (Fowler *et al.*, 1957; Rodman *et al.*, 1959) and (b) the tendency of the erythrocytes to sickle and occlude small vessels in the systemic and possibly the coronary circulation (Oliveira and Gomez-Patino, 1963; Rubler and Fleischer, 1967)

The performance of the left ventricle in these children with sickle cell anaemia was noninvasively evaluated by analysis of its echocardiographic dimensions throughout the cardiac cycle. As expected, increased end-diastolic left ventricular dimension and, therefore, volume as well as increased calculated cardiac output, were found in our group 2 symptomatic patients. In addition, and most importantly, in about one-third (15/44) of our patients, one or more previously established echocardiographic indices of left ventricular performance reflecting the extent (% ΔD, EF) or the velocity (Vcf) of shortening of myocardial fibres during ejection were found to be significantly depressed to levels lower than the lowest values observed in normal subjects of comparable age. All these patients had dyspnoea and/or fatigue on mild effort and cardiomegaly on *x*-ray, but these findings were also present in the remaining 20 patients of group 2 whose left ventricular performance was found to be normal. Thus, identification of left ventricular dysfunction coexisting with, and concealed by the non-cardiac circulatory congestion attributable to the severe anaemia (Eichna, 1960), was feasible by echocardiography but not by clinical methods, or—in view of the almost universal cardiomegaly observed in our symptomatic patients—by routine radiological techniques. Though this study indicated the presence of depressed left ventricular performance in a proportion of patients with sickle cell anaemia the noninvasive nature of our methods precluded determination of the aetiological factors responsible for, or the mechanisms involved in, its production.

Our findings are in obvious contrast with those recently reported by Gerry *et al.* (1976) who found no evidence of left ventricular myocardial dysfunction in adults with sickle cell anaemia studied by echocardiography. The echocardiographic indices and the degree of anaemia (haematocrit) in the populations of both studies were similar. Subdivision of their patients into two age groups ($43{\cdot}5 \pm 2{\cdot}6$ and $22{\cdot}1 \pm 0{\cdot}7$ years, mean $\pm$ standard deviation) failed to identify differences in left ventricular performance that would suggest progressive deterioration in heart function. The significant age difference, however, between that study's population and our patients may provide a possible explanation for the discrepancy in the findings. Thus, it is reasonable to assume that patients with sickle cell anaemia who develop left ventricular failure detectable by echocardiography at a younger age, are more likely to die before reaching adulthood so they are naturally eliminated and, therefore, not represented in the older age groups that consist only of those subjects whose heart performance has never been compromised. The lack of difference in the degree of anaemia in the population of the two studies does not argue against this hypothesis since factors other than the severity of anaemia, for example, the extent and frequency of microthromboses in the coronary circulation (Oliveria and Gomez-Patino, 1963; Rubler and Fleischer, 1967), may also independently affect the capability of the left ventricle to compensate for the increased volume load imposed on it by the disease. A possible alternative to the above hypothesis is that the natural history of myocardial involvement in sickle cell anaemia is sporadic, and actual improvement may occur between childhood and adulthood.

In conclusion, this study has demonstrated the presence of depressed left ventricular performance in a significant proportion of symptomatic children with sickle cell anaemia. Echocardiography appears to be a useful technique which may provide guidance for specific treatment directed against heart failure coexisting with, and partially responsible for, the congestive circulatory state observed in children with severe sickle cell anaemia.

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Notice

International Committee on Thrombosis and Haemostasis

The XXIVth annual meeting of the International Committee on Thrombosis and Haemostasis will be held at the University of Leuven, Belgium, on 20-22 July 1978.

Further information and the registration form can be obtained from Dr M. Verstraete, Centre for Thrombosis and Vascular Research, Department of Medical Research, Campus Gasthuisberg, Herestraat 49, 3000 Leuven, Belgium.